REMARKS/ARGUMENTS

Reconsideration of this application and entry of the foregoing amendments are respectfully requested.

Claims 21, 22 and 24 have been revised to define the invention with additional clarity. The amendments to claims 22 and 24 are intended to make clear the terms "*in vivo*" and "*in vitro*" as used in accordance with the present specification. In the present specification, it is quite clear that the term "*in vitro*" is used to refer to a cellular free system. In contrast, the term "*in vivo*" is used to refer to an intracellular system. However, in both cases, the method is essentially "*in vitro*" as routinely used and it is not suggested that the present methods be carried out, for example, in a human or animal body. The recitation in the revised claims of cells or organisms that can be used in accordance with the invention finds support on page 25 of the subject specification. That the claims have been revised should not be taken as an indication that Applicants agree with any position taken by the Examiner.

Claims 21, 22, 24-29, 34-36, 39 and 40 stand rejected under 35 USC 112, first paragraph, as allegedly being non-enabled. Withdrawal of the rejection is submitted to be in order in view of the above-noted claim revisions and comments that follow.

The Examiner has raised a lack of enablement rejection with respect to an "*in vivo*" method using any type of organism using any cis-acting DNA binding protein. Applicants believe that the rejection arises, in part, because of confusion regarding the meaning of the terms "*in vitro*" and "*in vivo*". In particular, the Examiner refers to an "*in vitro*" method that uses a host cell. However, in the context of the present specification, the term "*in vitro*" is used to refer to a cell free system. For the avoidance of doubt, the claims as now presented make it additionally clear that the invention is either carried out in a cell free system or that it is carried

out in a cell system. In both cases, this is an "*in vitro*" system in the conventional use of the term "*in vitro*".

Expression of peptides in *in vitro* host systems is a matter of routine for one of skill in the art.

The present invention requires the expression of a desired library with a protein bound to its own encoding DNA by covalent binding. In the present invention, it is the use of the *cis*-acting DNA peptide or protein that achieves the binding of such a protein to its own encoding DNA through covalent binding. It is an inherent property of the *cis*-acting DNA peptide or protein. Thus, it would not be expected that this binding would be effected by the host cell in which the protein was expressed.

The Examiner has referred to page 9 of the specification to suggest that there is unpredictability in obtaining the necessary *cis*-action. However, the passage cited by the Examiner merely states that the mechanism by which this *cis*-action is achieved is not known. However, that is not the same as saying that the *cis*-action itself is not predictable.

In view of the above, reconsideration is requested.

Claims 21, 22, 24-29, 34-36, 39 and 40 stand rejected under 35 USC 103 as allegedly being obvious over Schatz in view of Derbyshire or Liu. The rejection is traversed for the reasons that follow.

As acknowledged by the Examiner, Schatz does not disclose the use of a *cis*-acting protein as the DNA-binding protein. Applicants submit that there is nothing in Schatz that would have suggested that such *cis*-acting proteins should be used. Further, nothing is seen in the cited art that would have motivated an artisan to combine the teachings of Schatz with those of

Derbyshire or Liu. The combination would appear to be based on improper hindsight-based reasoning, as evidenced by the Examiner's arguments.

Both Derbyshire and Liu are in an unrelated field to protein display and the production of peptide display libraries. Thus, Applicants cannot see why, absent knowledge of the present invention, these documents would have been combined by one of skill in the art as has been done by the Examiner. No suggestion for making that combination is found in the references themselves. Nothing in Derbyshire or Liu would have suggested that the proteins described in those documents might have any utility in such peptide display libraries.

The Examiner has highlighted two features of *cis*-acting proteins that are referred to in Derbyshire and Liu and suggests that the advantages in the use of *cis*-acting proteins in the method of Schatz is taught by Liu and Derbyshire. However, the statements referred to by the Examiner and quoted from Derbyshire and Liu do not suggest that there is any advantage of these particular proteins. The passages referred to by the Examiner do not suggest that there is any advantage in using *cis*-acting proteins as opposed to non-*cis*-acting proteins, such as those used in Schatz.

More specifically, the Examiner quotes the statement in Derbyshire on page 1261 which reads:

> *"A cis-acting protein can work up to 1000-fold more efficiently if its gene is located close to its binding site"*

This statement merely relates to *cis*-acting proteins *per se* and how such proteins might act in the most efficient manner. It does not suggest that *cis*-acting proteins might in some way be more efficient or have some advantage over the proteins described in Schatz. Derbyshire does not teach an advantage in the use of a *cis*-acting proteins but merely presents a statement of fact

relating to *cis*-acting proteins, namely that they work a 1000-fold more efficiently if its gene is located close to its binding site.

The Examiner make reference to the disclosure on page 163 in Liu. The relevant statement quoted by the Examiner reads as follows:

> *"The best studied system is that of the ssDNA phage ΦX174, where the A protein nicks the ori site in the viral strand of the replicative form and forms a covalent link to the 5' end of the cleaved strand."*

Thus, this statement does not suggest that there are any particular advantages of *cis*-acting proteins but merely identifies the best-studied *cis*-acting protein. There are no general statements in this document about the advantages of *cis*-acting proteins. For almost any class of proteins, there will be one protein that has been studied in more detail than any of the others. However, this cannot make the general class of proteins obvious in the light of a disclosure such as Schatz which does not suggest that that general class of proteins should be used.

In summary, the "advantages" of *cis*-acting proteins are simply that one *cis*-acting protein has been well studied (the disclosure of Liu) and that *cis*-acting proteins work more efficiently when their genes are located close to their binding sites. These are not advantages of cis-acting proteins compared to other DNA binding proteins, such as those described in Schatz. Thus, motivation to combine the teachings of Liu or Derbyshire with the teachings of Schatz is missing.

Applicants submit, therefore, that the claims would not have been obvious over Schatz in view of Liu or Derbyshire and reconsideration is requested..

LINDQVIST et al
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This application is submitted to be in condition for allowance and a Notice to that effect is requested.

Respectfully submitted,

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